

BEST AVAILABLE COPY

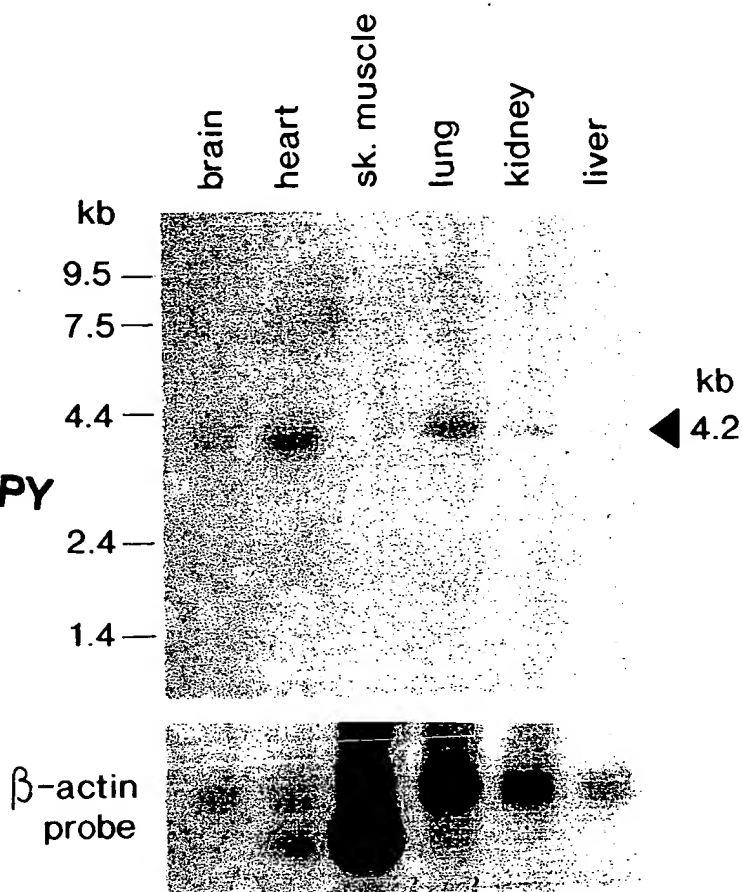


FIG. 11A

FIG. 11B

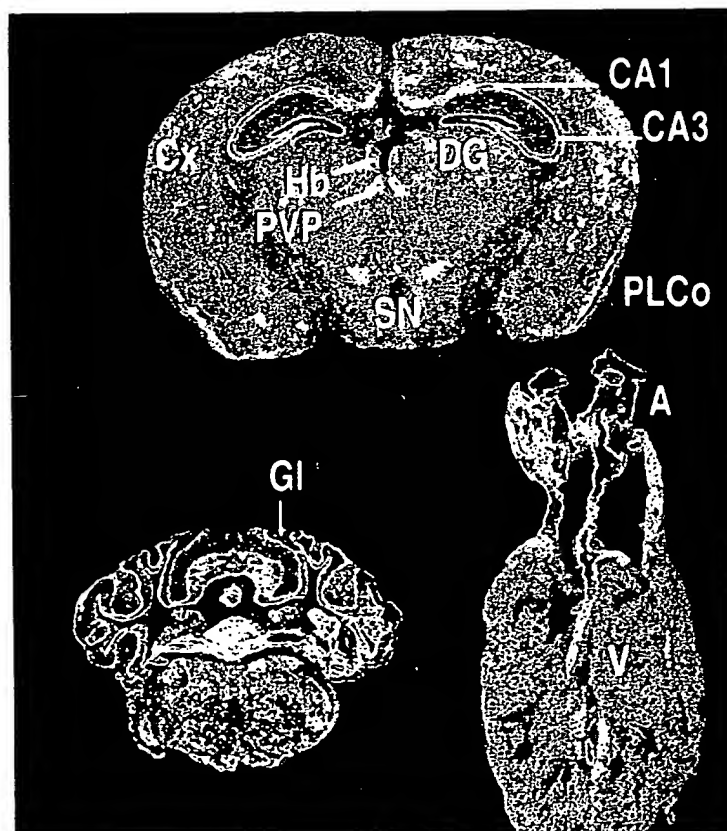


FIG. 11C

FIG. 11D

FOI280-4046560

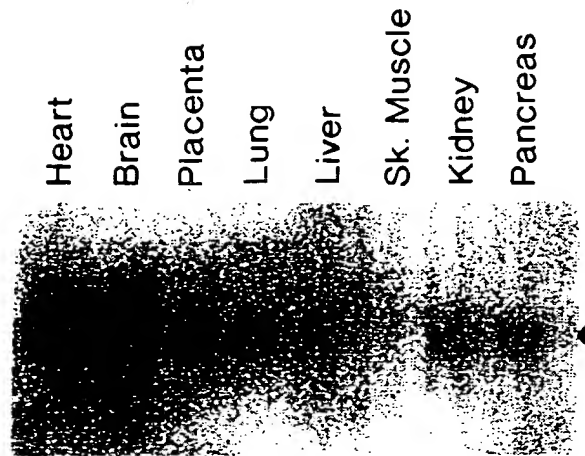


FIG. 1A

BEST AVAILABLE COPY

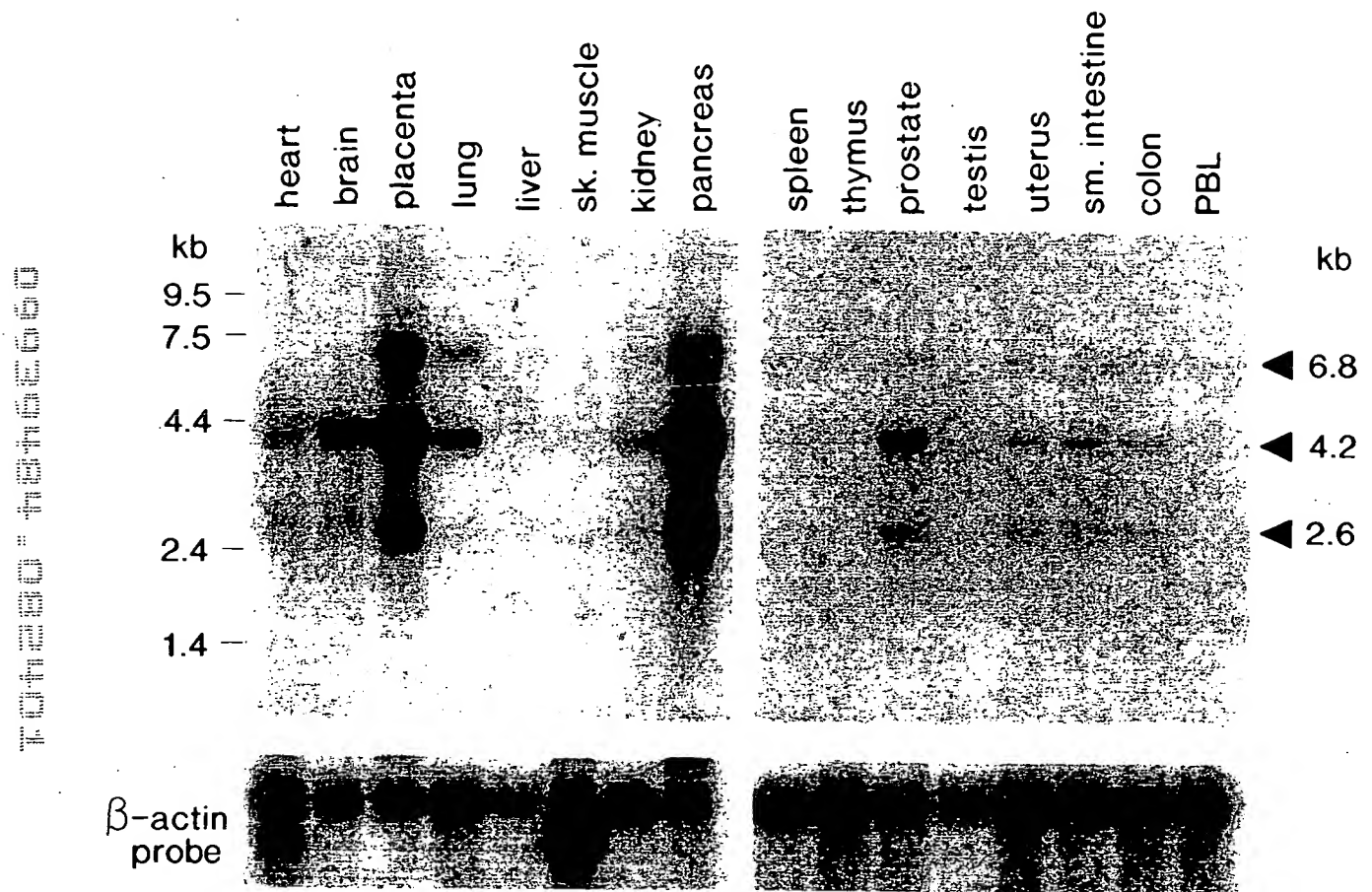


FIG. 10

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gggcaggaagacggcgctgcccgaggagc																				-153
ggggcgggcgggcgcgcgggggagcgggcgggcgggcgggagccagggccggcgggggcgggggcgggcgggccag																				-77
aagaggcgggcgggcgcgctccggccggtctcgggcggttgcccttggtttggctttggcgggcgggcggtggagaag																				-1
ATG	CTG	CAG	TCC	CTG	GCC	GGC	AGC	TCG	TGC	GTG	CGC	CTG	GTG	GAG	CGG	CAC	CGC	TCG		57
M	L	Q	S	L	A	G	S	S	C	V	R	L	V	E	R	H	R	S		19
GCC TGG TGC TTC GGC TTC CTG GTG CTG GGC TAC TTG CTC TAC CTG GTC TTC GGC GCA																				114
A	W	C	F	G	F	L	V	L	G	Y	L	L	Y	L	V	F	G	A		38
GTG GTC TTC TCC TCG GTG GAG CTG CCC TAT GAG GAC CTG CTG CGC CAG GAG CTG CGC																				171
V	V	F	S	S	V	E	L	P	Y	E	D	L	L	R	Q	E	L	R		57
AAG CTG AAG CGA CGC TTC TTG GAG GAG CAC GAG TGC CTG TCT GAG CAG CAG CTG GAG																				228
K	L	K	R	R	F	L	E	E	H	E	C	L	S	E	Q	Q	L	E		76
CAG TTC CTG GGC CGG GTG CTG GAG GCC AGC AAC TAC GGC GTG TCG GTG CTC AGC AAC																				285
Q	F	L	G	R	V	L	E	A	S	N	Y	G	V	S	V	L	S	N		95
GCC TCG GGC AAC TGG AAC TGG GAC TTC ACC TCC GCG CTC TTC TTC GCC AGC ACC GTG																				342
A	S	G	N	W	N	W	D	F	T	S	A	L	F	F	A	S	T	V		114
CTC TCC ACC ACA GGT TAT GGC CAC ACC GTG CCC TTG TCA GAT GGA GGT AAG GCC TTC																				399
L	S	T	T	G	Y	G	H	T	V	P	L	S	D	G	G	K	A	F		133
TGC ATC ATC TAC TCC GTC ATT GGC ATT CCC TTC ACC CTC CTG TTC CTG ACG GCT GTG																				456
C	I	I	Y	S	V	I	G	I	P	F	T	L	L	F	L	T	A	V		152
GTC CAG CGC ATC ACC GTG CAC GTC ACC CGC AGG CCG GTC CTC TAC TTC CAC ATC CGC																				513
V	Q	R	I	T	V	H	V	T	R	R	P	V	L	Y	F	H	I	R		171
TGG GGC TTC TCC AAG CAG GTG GTG GCC ATC GTC CAT GCC GTG CTC CTT GGG TTT GTG																				570
W	G	F	S	K	Q	V	V	A	I	V	H	A	V	L	L	G	F	V		190
ACT GTG TCC TGC TTC TTC TTC ATC CCG GCC GCT GTC TTC TCA GTC CTG GAG GAT GAC																				627
T	V	S	C	F	F	F	I	P	A	A	V	F	S	V	L	E	D	D		209

FIG. 1B-1

TGG AAC TTC CTG GAA TCC TTT TAT TTT TGT TTT ATT TCC CTG AGC ACC ATT GGC CTG	684
W N F L E S F Y F C F I S L S T I G L	228
GGG GAT TAT GTG CCT GGG GAA GGC TAC AAT CAA AAA TTC AGA GAG CTC TAT AAG ATT	741
G D Y V P G E G Y N Q K F R E L Y K I	247
GGG ATC ACG TGT TAC CTG CTA CTT GGC CTT ATT GCC ATG TTG GTA GTT CTG GAA ACC	798
G I T C Y L L L G L I A M L V V L E T	266
TTC TGT GAA CTC CAT GAG CTG AAA AAA TTC AGA AAA ATG TTC TAT GTG AAG AAG GAC	855
F C E L H E L K K F R K M F Y V K K D	285
AAG GAC GAG GAT CAG GTG CAC ATC ATA GAG CAT GAC CAA CTG TCC TTC TCC TCG ATC	912
K D E D Q V H I I E H D Q L S F S S I	304
ACA GAC CAG GCA GCT GGC ATG AAA GAG GAC CAG AAG CAA AAT GAG CCT TTT GTG GCC	969
T D Q A A G M K E D Q K Q N E P F V A	323
ACC CAG TCA TCT GCC TGC GTG GAT GGC CCT GCA AAC CAT TGA gcgtaggatttgttgcatt	1030
T Q S S A C V D G P A N H *	337
atgctagagcaccaggggtcaggggtgcaaggaagaggttaagtatgttcattttttatcagaatgcaaaagcgaaaa	1106
ttatgtcactttaagaaatagctactgtttgcaatgtcttattaaaaaacaacaaaaaagacacatggaacaaag	1182
aagctgtgaccccagcaggatgtctaataatgtgaggaaatgagatgtccacctaataattcatatgtgacaaaatta	1258
tctcgaccttacataggaggagaataacttgaagcagtatgctgctgtggttagaagcagattttatacttttaact	1334
ggaaactttgggggttgcathtagatcatttagctgatggctaaatagcaaaatttatatttagaagcaaaaaaaa	1410
aaagcatagagatgtgtttataaatagggttatgtgtactggtttgcatgtaccacccaaaatgattatttttg	1486
gagaatctaagtcaaactcactatttataatgcataggtaaccattaactatgtacatataaagtataaatatgtt	1562
tatattctgtacatatggtttaggtcaccagatcctagtgtagtcttgaaactaagactatagatattttgtttct	1638
tttgatttctctttataactaaagaatccagagttgctacaataaaataaggggaataataaaaaaaaaaaaaa	1712

FIG. 1B-2

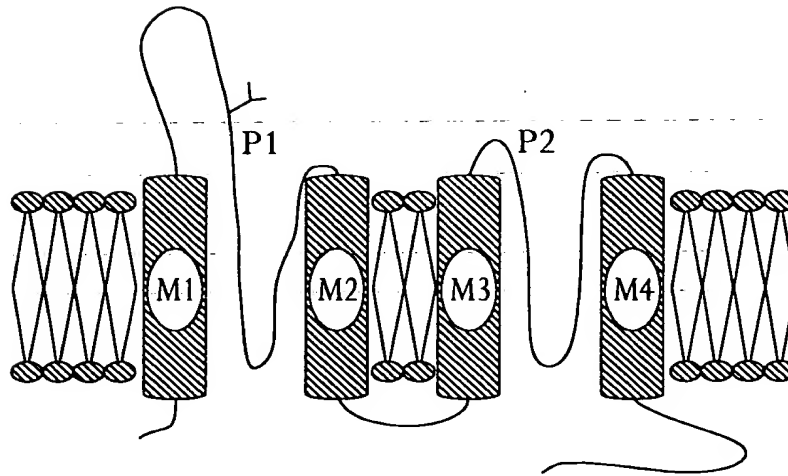
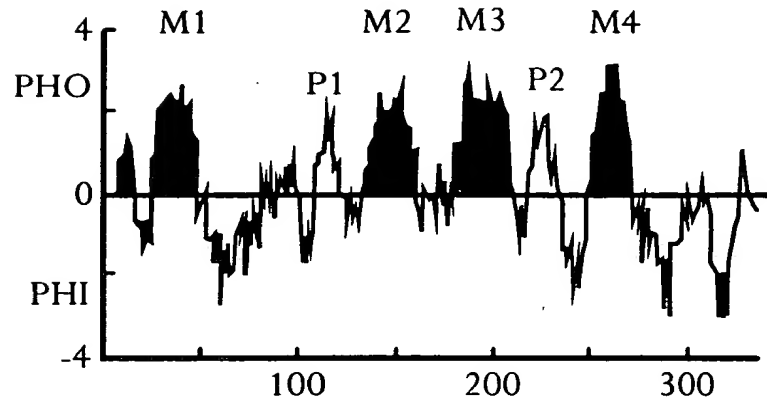


FIG. 1C

1201-CIP-DIV-00

	1	14	27
TWIK-1 P1	F	T	S
TWIK-1 P2	F	L	E
TOK1 P2	Y	F	N
TOK1 P1	Y	G	N
Slo	Y	W	T
Shaker	I	P	D
Shab	I	P	E
Shal	I	P	A
Shaw	I	P	L
KAT1	Y	V	T
AKT1	Y	V	T
eag	Y	V	T
ROMK1	M	T	S
IRK1	F	T	A
GIRK1	F	P	S

FIG. 2A

**FIG. 2B**



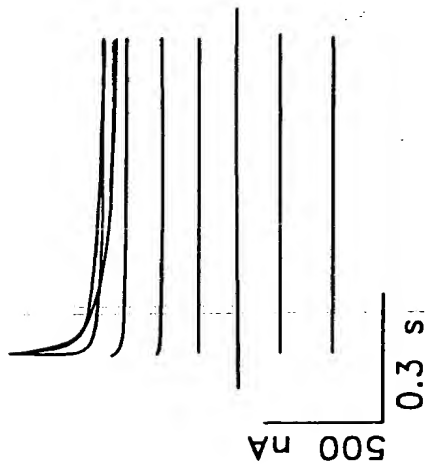


FIG. 3A

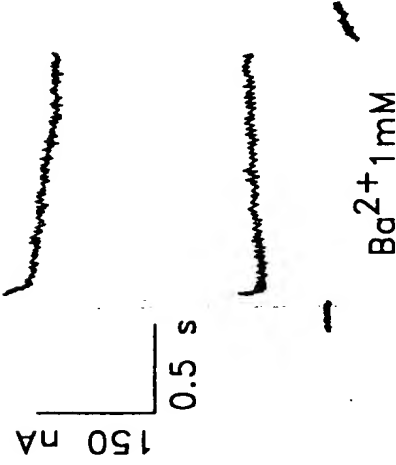


FIG. 3D

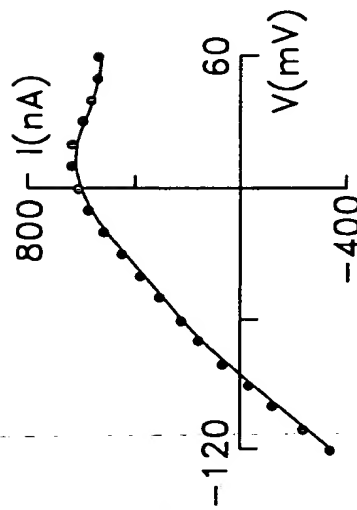


FIG. 3B

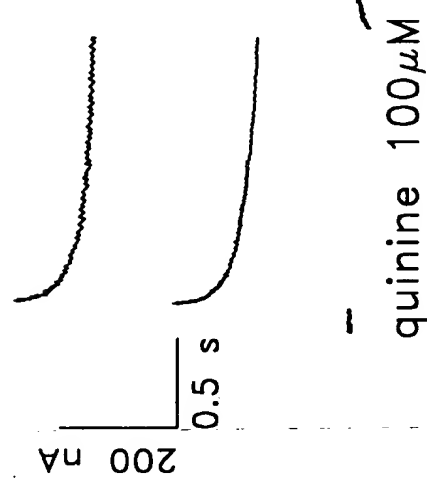


FIG. 3E

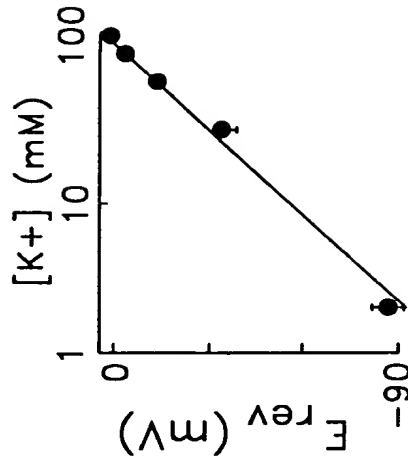


FIG. 3C

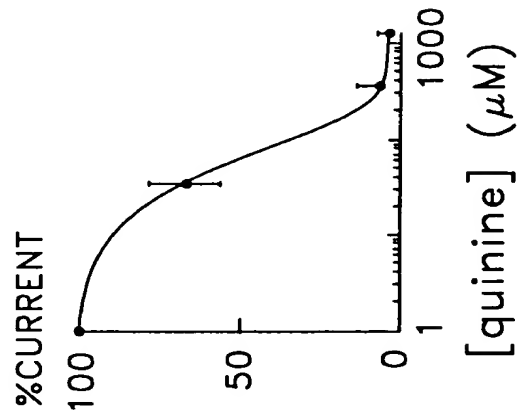


FIG. 3F

FIG. 4A

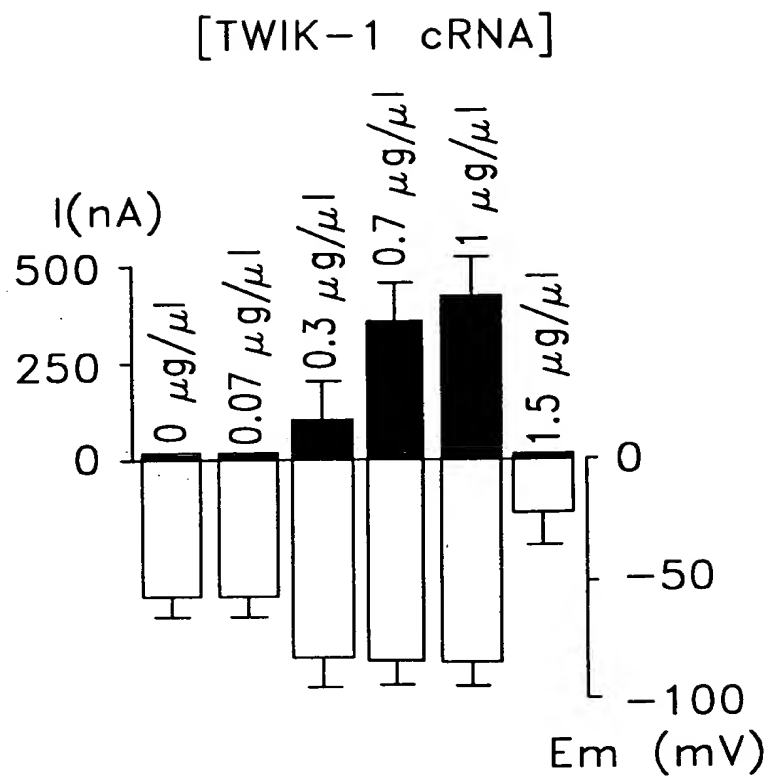


FIG. 4B

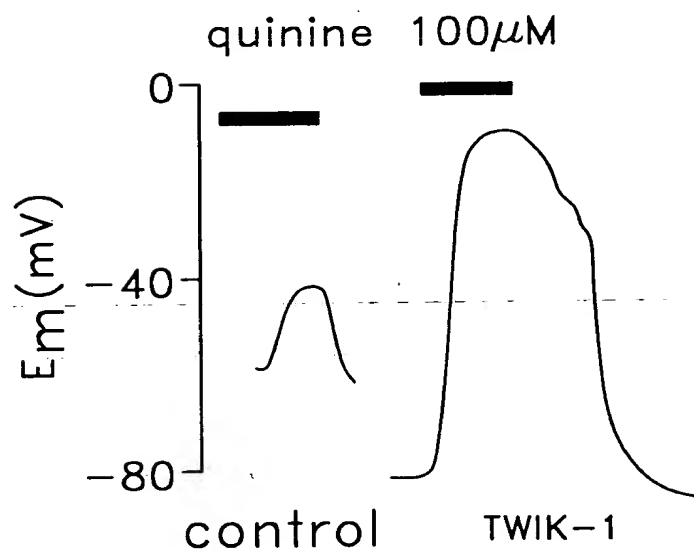
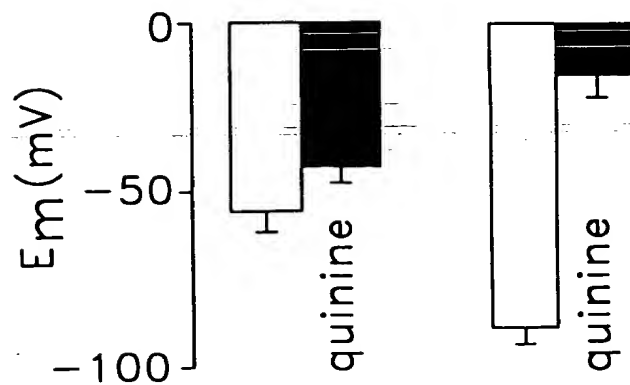


FIG. 4C



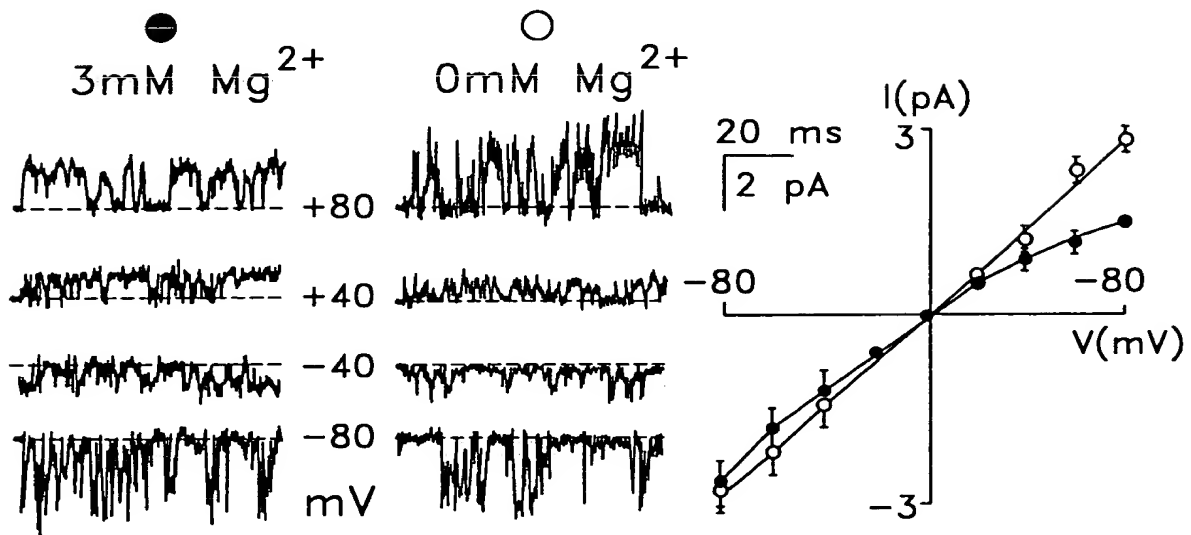


FIG. 5A

FIG. 5B

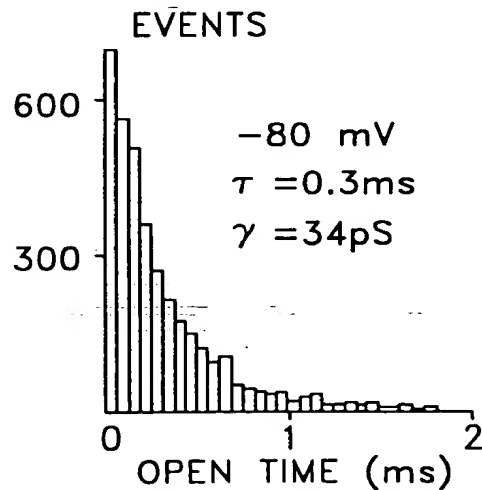
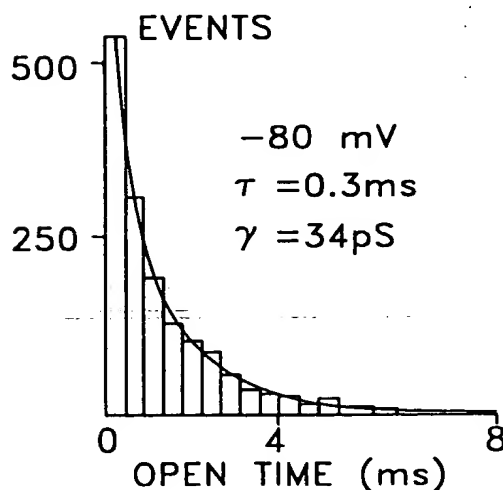
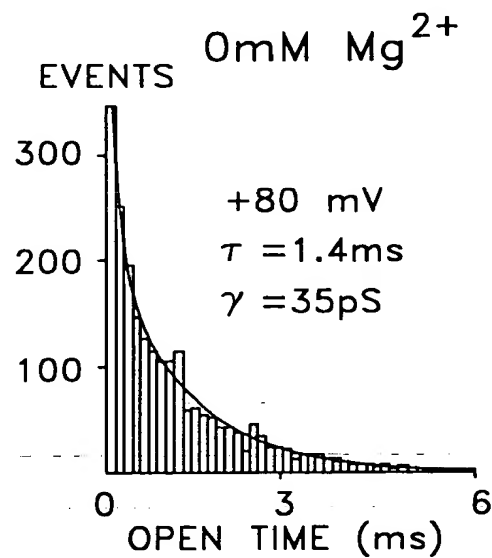
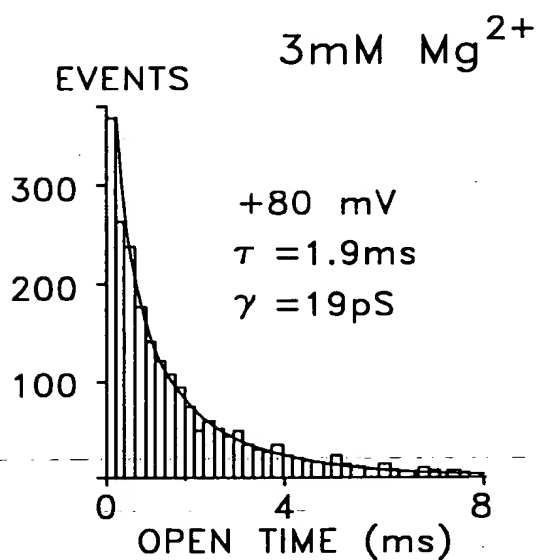


FIG. 5C

FIG. 5D

000394-082401

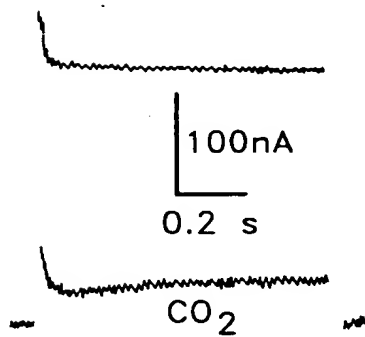


FIG. 6A

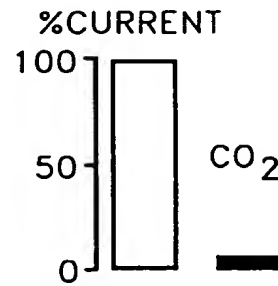


FIG. 6B

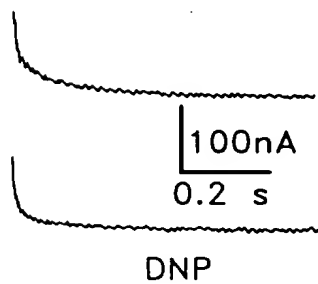


FIG. 6C

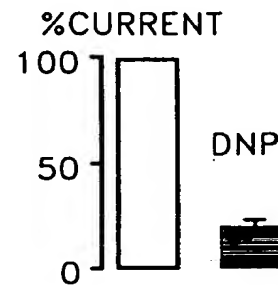


FIG. 6D

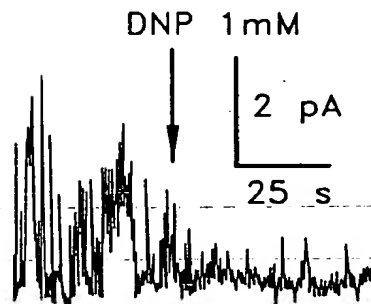


FIG. 6E

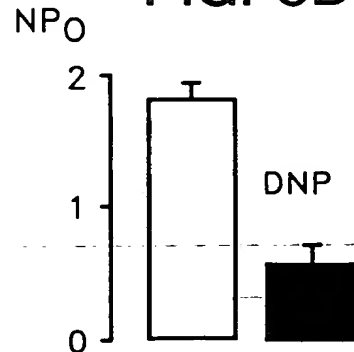


FIG. 6F

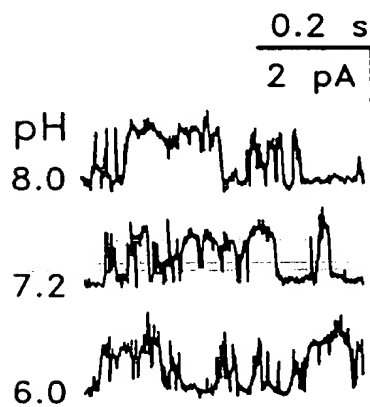


FIG. 6G

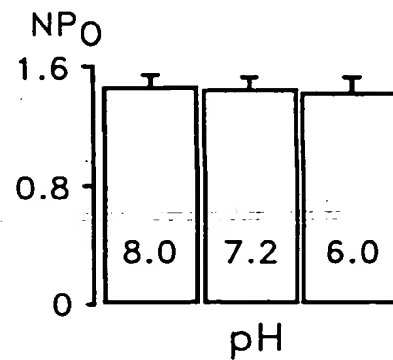


FIG. 6H

101280-14102660

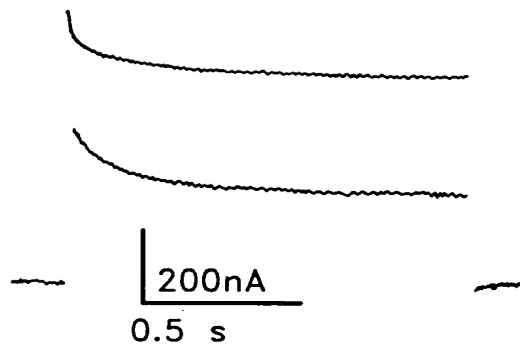


FIG. 7A

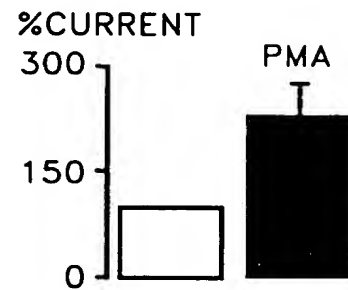


FIG. 7B

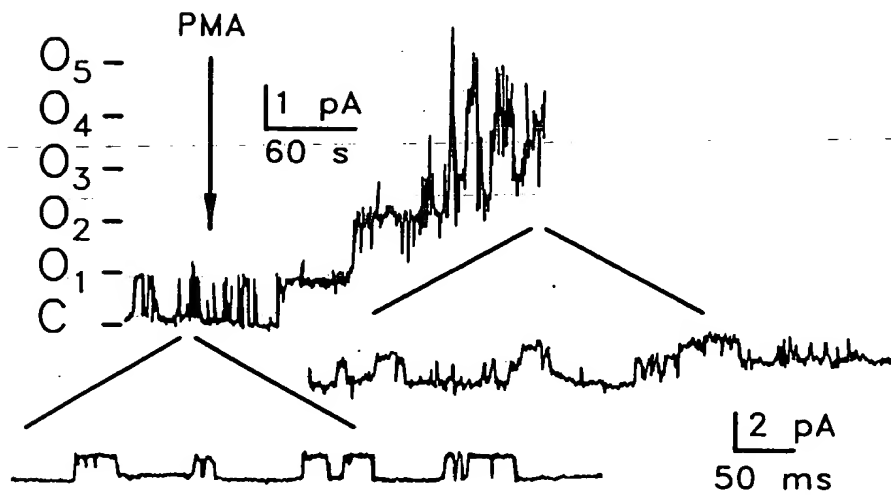


FIG. 7C

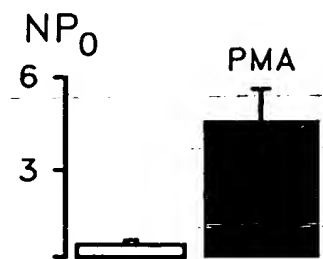


FIG. 7D

tgccctgcgcggatagcggcgagcgcagccatgccccaggccgcctccg -77  
 gggcagcagcagcggcgccggggccgatgcgcggggccggggcgccggggggccggcgggccggggcggggacg -1

ATG AAG CGG CAG AAC GTG CGC ACG CTG GCG CTC ATC GTG TGC ACC TTC ACC TAC CTG 57  
 M K R Q N V R T L A L I V C T F T Y L 19  
 E N V R T L A L I V C T F T Y L

CTG GTG GGC GCC GCG GTC TTC GAC GCG CTG GAG TCG GAG CCC GAG CTG ATC GAG CGG 114  
 L V G A A V F D A L E S E P E L I E R 38  
 L V G A A V F D A L E S E P E M I E R

CAG CGG CTG GAG CTG CGG CAG CAG GAG CTG CGG GCG CGC TAC AAC CTC AGC CAG GGC 171  
 Q R L E L R Q Q E L R A R Y N L S Q G 57  
 Q R L E L R Q L E L R A R Y N L S E G  
 \*

GGC TAC GAG GAG CTG GAG CGC GTC GTG CTG CGC CTC AAG CCG CAC AAG GCC GGC GTG 228  
 G Y E E L E R V V L R L K P H K A G V 76  
 G Y E E L E R V V L R L K P H K A G V

CAG TGG CGC TTC GCC GGC TCC TTC TAC TTC GCC ATC ACC GTC ATC ACC ACC ATC GGC 285  
 Q W R F A G S F Y F A I T V I T T I G 95  
 Q W R F A G S F Y F A I T V I T T I G

TAC GGG CAC GCG GCA CCC AGC ACG GAT GGC GGC AAG GTG TTC TGC ATG TTC TAC GCG 342  
 Y G H A A P S T D G G K V F C M F Y A 114  
 Y G H A A P S T D G G K V F C M F Y A

CTG CTG GGC ATC CCG CTC ACG CTC GTC ATG TTC CAG AGC CTG GGC GAG CGC ATC AAC 399  
 L L G I P L T L V M F Q S L G E R I N 133  
 L L G I P L T L I M F Q S L G E R I N

ACC TTG GTG AGG TAC CTG CTG CAC CGC GCC AAG AAG GGG CTG GGC ATG CGG CGC GCC 456  
 T L V R Y L L H R A K K G L G M R R A 152  
 T E V R Y L L H R A K B G L G M R H A

GAC GTG TCC ATG GCC AAC ATG GTG CTC ATC GGC TTC TTC TCG TGC ATC AGC ACG CTG -513  
 D V S M A N M V L I G F F S C I S T L 171  
 E V S M A N M V L I G F V S C I S T L

TGC ATC GGC GCC GCC GGC TTC TCC CAC TAC GAG CAC TGG ACC TTC TTC CAG GCC TAC 570  
 C I G A A A F S H Y E H W T F F Q A Y 190  
 C I G A A A F S Y Y E B W T F F Q A Y

TAC TAC TGC TTC ATC ACC CTC ACC ACC ATC GGC TTC GGC GAC TAC GTG GCG CTG CAG 627  
 Y Y C F I T L T T I G F G D Y V A L Q 209  
 Y Y C F I T L T T I G F G D Y V A L Q

AAG GAC CAG GCC CTG CAG ACG CAG CCG CAG TAC GTG GCC TTC AGC TTC GTC TAC ATC 684  
 K D Q A L Q T Q P Q Y V A F S F V Y I 228  
 K D Q A L Q T Q P Q Y V A F S F V Y I

CTT ACG GGC CTC ACG GTC ATC GGC GCC TTC CTC AAC CTC GTG GTG CTG CGC TTC ATG 741  
 L T G L T V I G A F L N L V V L R F M 247  
 L T G L T V I G A F L N L V V L R F M

FIG. 8A

ACC	ATG	AAC	GCC	GAG	GAC	GAG	AAG	CGC	GAC	GCC	GAG	CAC	CGC	GCG	CTG	CTC	ACG	CGC	798
T	M	N	A	E	D	E	K	R	D	A	E	H	R	A	L	L	T	R	266
T	M	N	A	E	D	E	K	R	D	A	E	H	R	A	L	L	T	H	
AAC	GGG	CAG	GCG	GGC	GGC	GGC	GGA	GGG	GGT	GGC	AGC	GCG	CAC	ACT	ACG	GAC	ACC	GCC	855
N	G	Q	A	G	G	G	G	G	G	G	S	A	H	T	T	D	T	A	285
N	G	Q	A	V	G	L	G	G	L	S	C	L	S	G	S	L	G	D	
TCA	TCC	ACG	GCG	GCA	GCG	GGC	GGC	GGC	GGC	TTC	CGC	AAC	GTC	TAC	GCG	GAG	GTG	CTG	912
S	S	T	A	A	A	G	G	G	G	F	R	N	V	Y	A	E	V	L	304
<u>VRPRDPV</u>	<u>TC</u>	<u>AA</u>	A	A	G	<u>GVGVGVGGS</u>	G	F	R	N	V	Y	A	E	V	L			
CAC	TTC	CAG	TCC	ATG	TGC	TCG	TGC	CTG	TGG	TAC	AAG	AGC	CGC	GAG	AAG	CTG	CAG	TAC	969
H	F	Q	S	M	C	S	C	L	W	Y	K	S	R	E	K	L	Q	Y	323
H	F	Q	S	M	C	S	C	L	W	Y	K	S	R	E	K	L	Q	Y	
TCC	ATC	CCC	ATG	ATC	ATC	CCG	CGG	GAC	CTC	TCC	ACG	TCC	GAC	ACG	TGC	GTG	GAG	CAG	1026
S	I	P	M	I	I	P	R	D	L	S	T	S	D	T	C	V	E	Q	342
S	I	P	M	I	I	P	R	D	L	S	T	S	D	T	C	V	E	H	
AGC	CAC	TCG	TCG	CCG	GGA	GGG	GGC	GGC	CGC	TAC	AGC	GAC	ACG	CCC	TCG	CGA	CGC	TGC	1083
S	H	S	S	P	G	G	G	G	R	Y	S	D	T	P	S	R	R	C	361
S	H	S	S	P	G	G	G	G	R	Y	S	D	T	P	S	H	P	C	
CTG	TGC	AGC	GGG	GCG	CCA	CGC	TCC	GCC	ATC	AGC	TCG	GTG	TCC	ACG	GGT	CTG	CAC	AGC	1140
L	C	S	G	A	P	R	S	A	I	S	S	V	S	T	G	L	H	S	380
L	C	S	G	T	Q	R	S	A	I	S	S	V	S	T	G	L	H	S	
CTG	TCC	ACC	TTC	CGC	GGC	CTC	ATG	AAG	CGC	AGG	AGC	TCC	GTG	TGA	ctgccccgaggggacc				1200
L	S	T	F	R	G	L	M	K	R	R	S	S	V	*					395
L	A	A	F	R	G	L	M	K	R	R	S	S	V						
tggagc	acactg	ggggcg	cgggcg	ggggcg	ggggcg	ggggcg	ggggcg	ggggcg	ggggcg	ggggcg	ggggcg	ggggcg	ggggcg	ggggcg	ggggcg	ggggcg	ggggcg	ggggcg	1276
ggacccc	gcacaa	catccc	ctcacc	actctc	ccccag	caccccc	atctcc	gactgt	gcctgt	gttgca	caccag	ccggca							1352
ggaggcc	ggggtc	tctgag	gacccc	ctgggg	ccccat	cggagc	ccctgca	aatccg	agaaat	gtgaa	acttgg	tgggg							1428
tcaggga	ggaaag	gcaga	agctgg	ggagcc	ctccct	ctcttg	aaaatc	taaga	agctccc	agtcct	cagag	acct							1504
gctggt	accacac	ccccac	cttcgg	agggga	cttcatt	gttcct	gtgac	gtttgc	atctct	attata	acctct	gtcct							1580
gctaggt	ctccac	cttccct	tggttc	caaaag	ccagggt	gtctat	gtcca	agtcaccc	ctactc	agcccc	actcc								1656
cttctct	catcccc	agctgt	gtctcc	caacct	cccttc	gtgtgt	ttttgc	atggct	tttgc	agttat	ggagaa	agtg							1732
gaaaccc	agcagtc	ccctaa	agctgg	tcccc	agaaag	caggac	agaaag	aggagg	ggacagg	gcagc	agggagg								1808
gcgagct	gggagg	caggag	gcgcgc	ctgtc	agtcgt	gcaga	atggtc	gcactg	ggaggt	tcaag	ctaact	ggcctc							1884
cagccac	attctc	atagc	aggtagg	acttc	cagcct	tccaga	caactg	cccttag	aatctg	gaacag	aagact	tcaga							1960
ctcacc	ataatt	gtgata	attaccc	actctt	aaattt	gtcgag	tgattt	ttagc	ctctg	aaaact	ctatgt	ctggc							2036
cactgat	tccttt	gagctc	acaaa	accctac	ttaggt	catcag	ggcagg	aggttct	cactccc	attttac	agatga								2112
gaatact	gagccct	ggacag	gtgaag	tgacc	agagca	aaaggc	aaaggc	tgggg	gctggg	tcagtc	gggtcac								2188
acctgt	attccca	caactt	ttgg	aggctg	agggtg	ggagg	attgct	tgagcc	aggga	attcg	agacc	agcctag	gtg						2264
acatagt	gagacccc	atctct	acaaaa	ataaaaa	ataacc	aggtgt	gggtgg	cacgtg	ccctggg	agtcacc	agcga								2340
cttggg	aggctg	agggtg	ggagg	attgtt	tgagc	ctggg	aggtcg	aggctg	tagtg	agccctg	attgc	accactg	ta						2416
ctccag	cctggg	tgacagg	ggaag	accctg	ctca	aaaaaaaa													2465

FIG. 8B

**FIG. 9A**

**FIG. 9B**



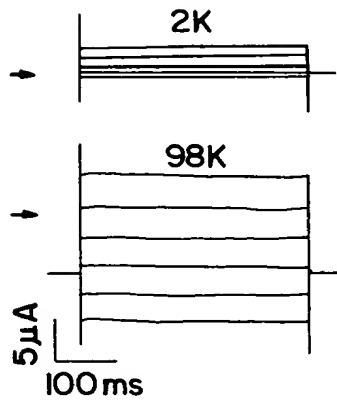


FIG. 12A

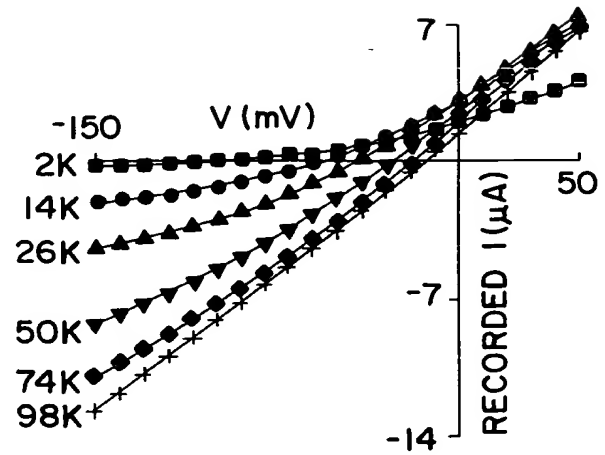


FIG. 12B

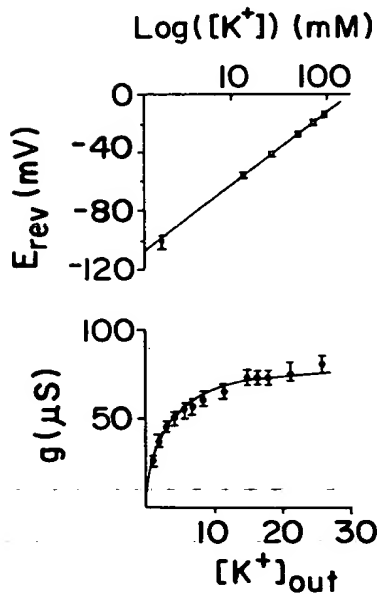


FIG. 12C

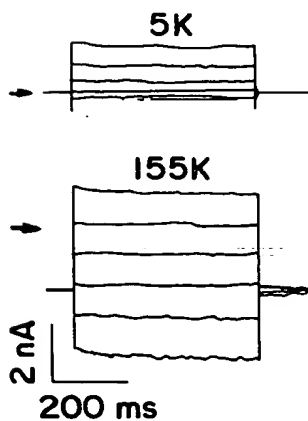


FIG. 12E

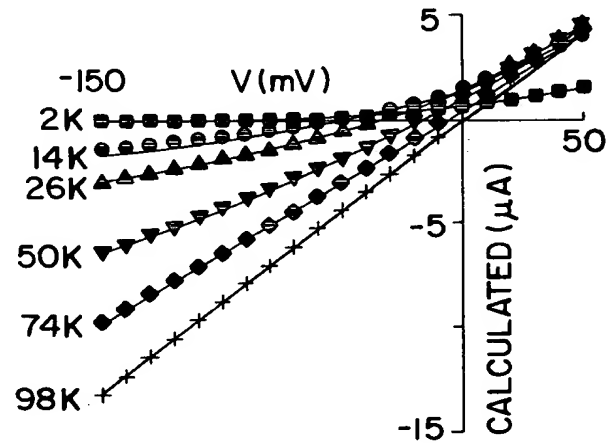


FIG. 12D

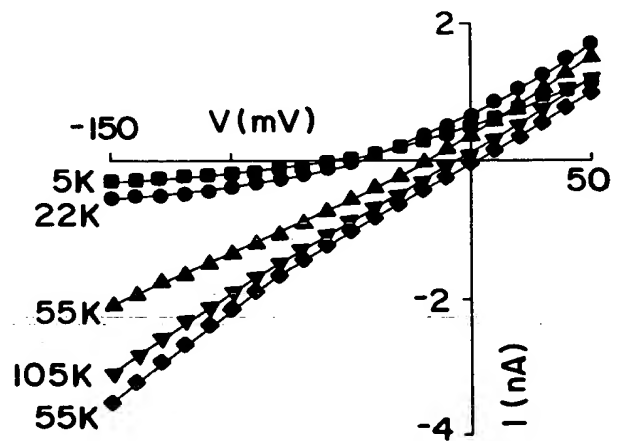


FIG. 12F

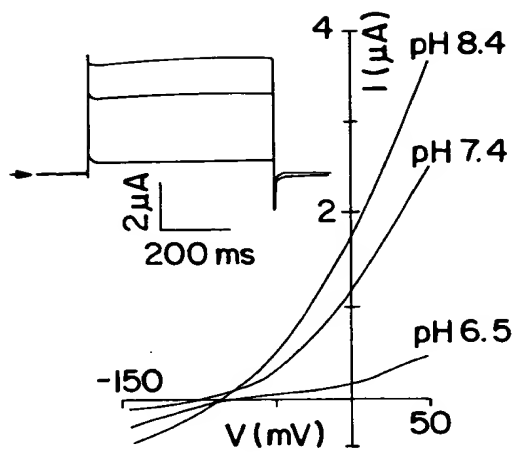


FIG. 13A

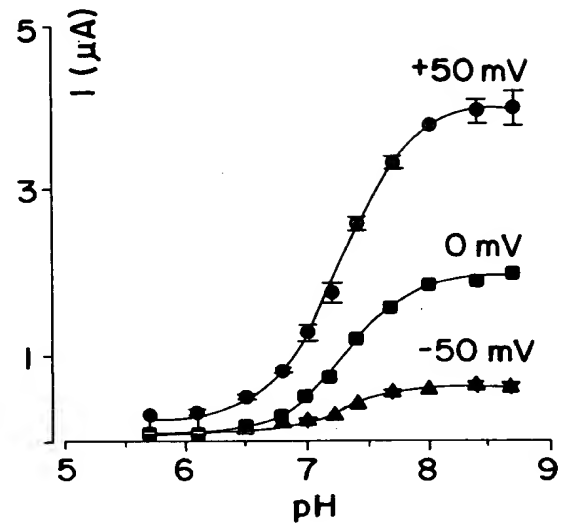


FIG. 13B

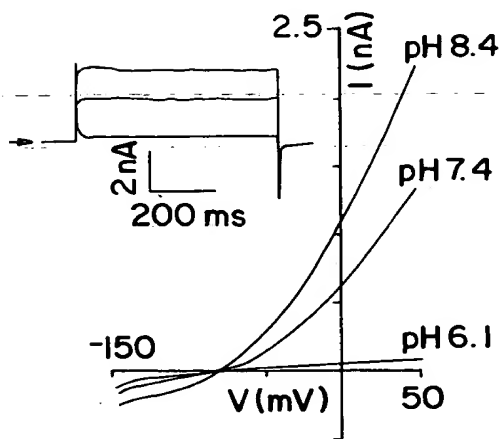


FIG. 13C

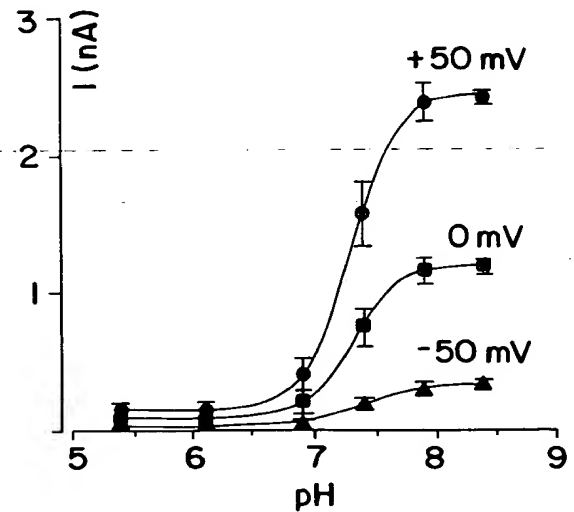


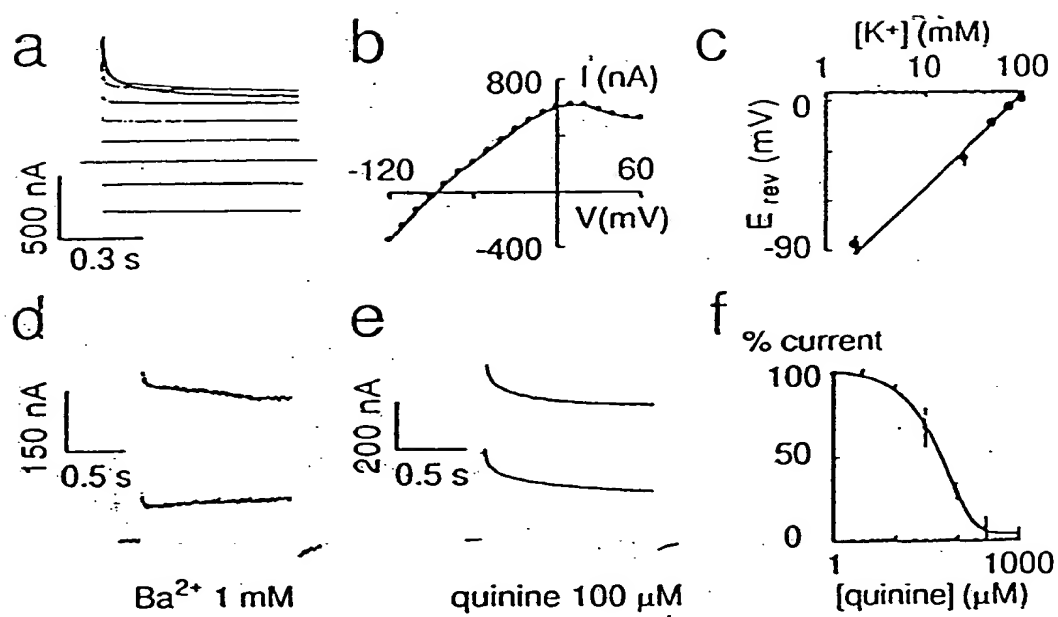
FIG. 13D



Fig. 2

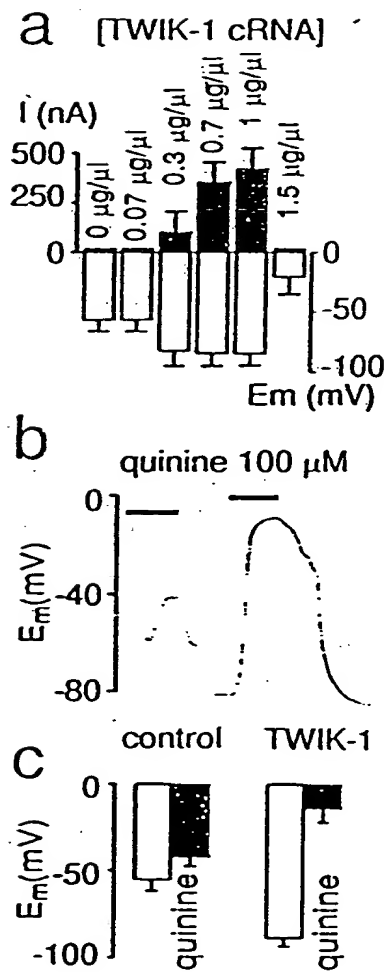
		1	14	27
a	TWIK-1 P1	RTSALEFFASTVLSTTGYGHTVPLSDGG		
	TWIK-1 P2	RLSEFVFCFESLSTTGLGDIYVPGEGYN		
	TOKI P2	VFNCIYFCFICLLTIGYGDYAPRTGAG		
	TOKI P1	YGNALYFCTVSLTTLVGLGDLPKSVGA		
	Sho	YWTCVYFLIVTSTTVGYGDMCETVLG		
	Shaker	IPDAFWMAMVTMTTVGYGDMTEVGFWG		
	Shab	IPEAFWMAGTMTTVGYGDMCPTTALG		
	Shal	IPAAFWMIVTMTTVGYGDMVPETTAG		
	Shaw	IPLLELWALVTMTTVGYGDMAPKTKIG		
	KATI	VVTALYVSTITLTTTGYGDFHAENPRE		
	AKTI	VVTSMYVSTITLTTVGYGDMHVPNTKE		
	cag	VVTALYVSTTCMTTVGYGDMMAAETDNE		
	ROMKI	MTSAFLFSGTQVTIGYGFRRVTEQCA		
	IRKI	RTAAFLFSIETQTTGYGFRCVTDECPC		
	GIRKI	RTSAFLFFIETEATGYGYRVTITDKCP		
b	TWIK-1	1	27	
	(17c8)	1	27	
	M110-2	1	27	
	TWIK-1	31	47	
	(17c8)	31	47	
	M110-2	49	65	
	TWIK-1	71	87	
	(17c8)	69	85	
	M110-2	96	112	
	P1			
	TWIK-1	110	126	
	(17c8)	115	131	
	M110-2	142	158	
	TWIK-1	157	173	
	(17c8)	162	178	
	M110-2	189	205	
	P2			
	TWIK-1	197	213	
	(17c8)	209	225	
	M110-2	213	229	
	TWIK-1	239	255	
	(17c8)	254	270	
	M110-2	253	269	
	TWIK-1	278	294	
	(17c8)	295	311	
	M110-2	294	310	
	TWIK-1	315	331	
	(17c8)	338	354	
	M110-2	342	358	

Fig. 3



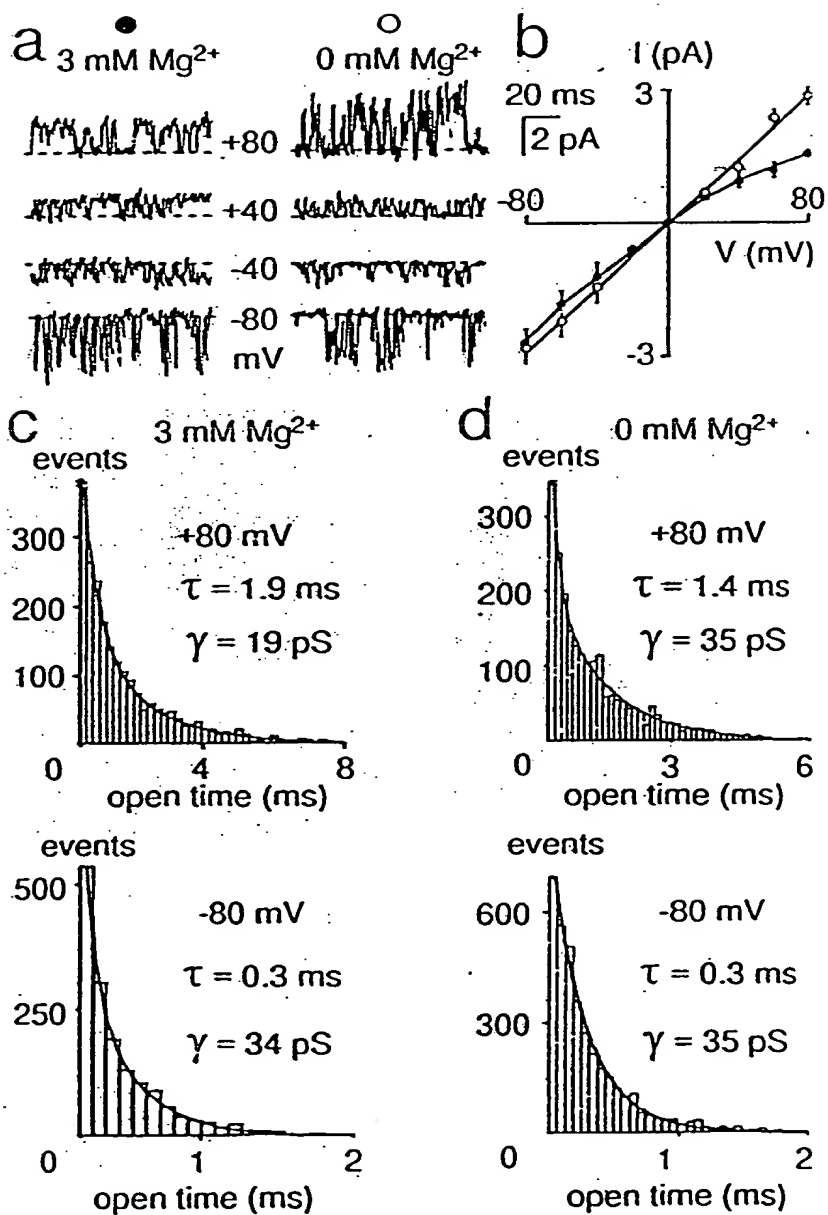
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Fig. 4



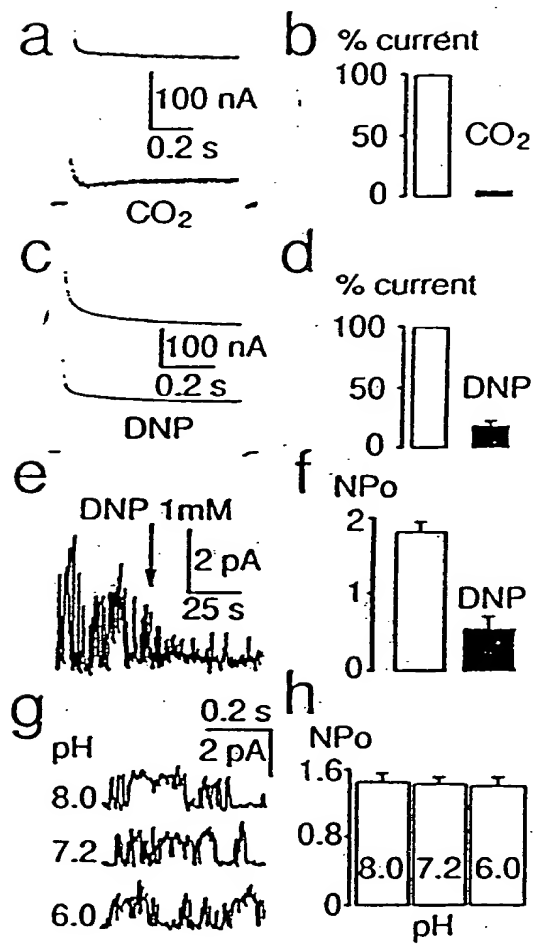
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Fig. 5



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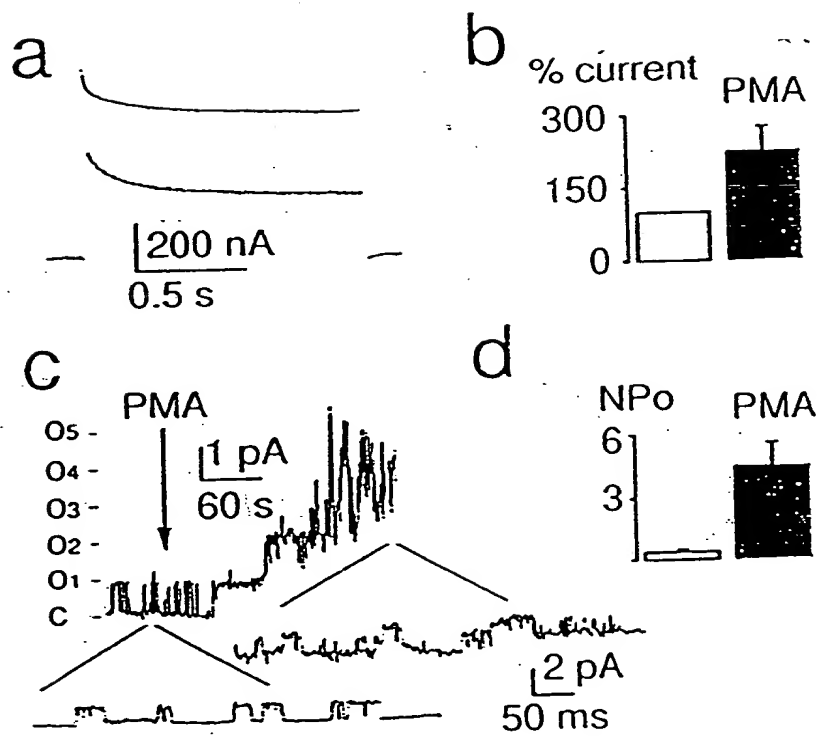
Fig. 6





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Fig. 7



[illegible]

[illegible]

[illegible]

The diagram illustrates the topology of a protein with four transmembrane domains. The N-terminus (NH<sub>2</sub>) is on the left, followed by a large extracellular loop. The first transmembrane domain is M1, with an extracellular loop P1. The second is M2, followed by an intracellular loop. The third is M3, followed by an extracellular loop P2. The fourth is M4, with an intracellular loop. The C-terminus (COOH) is on the right. Arrows indicate the 'out' and 'in' orientations relative to the membrane.

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Fig. 10

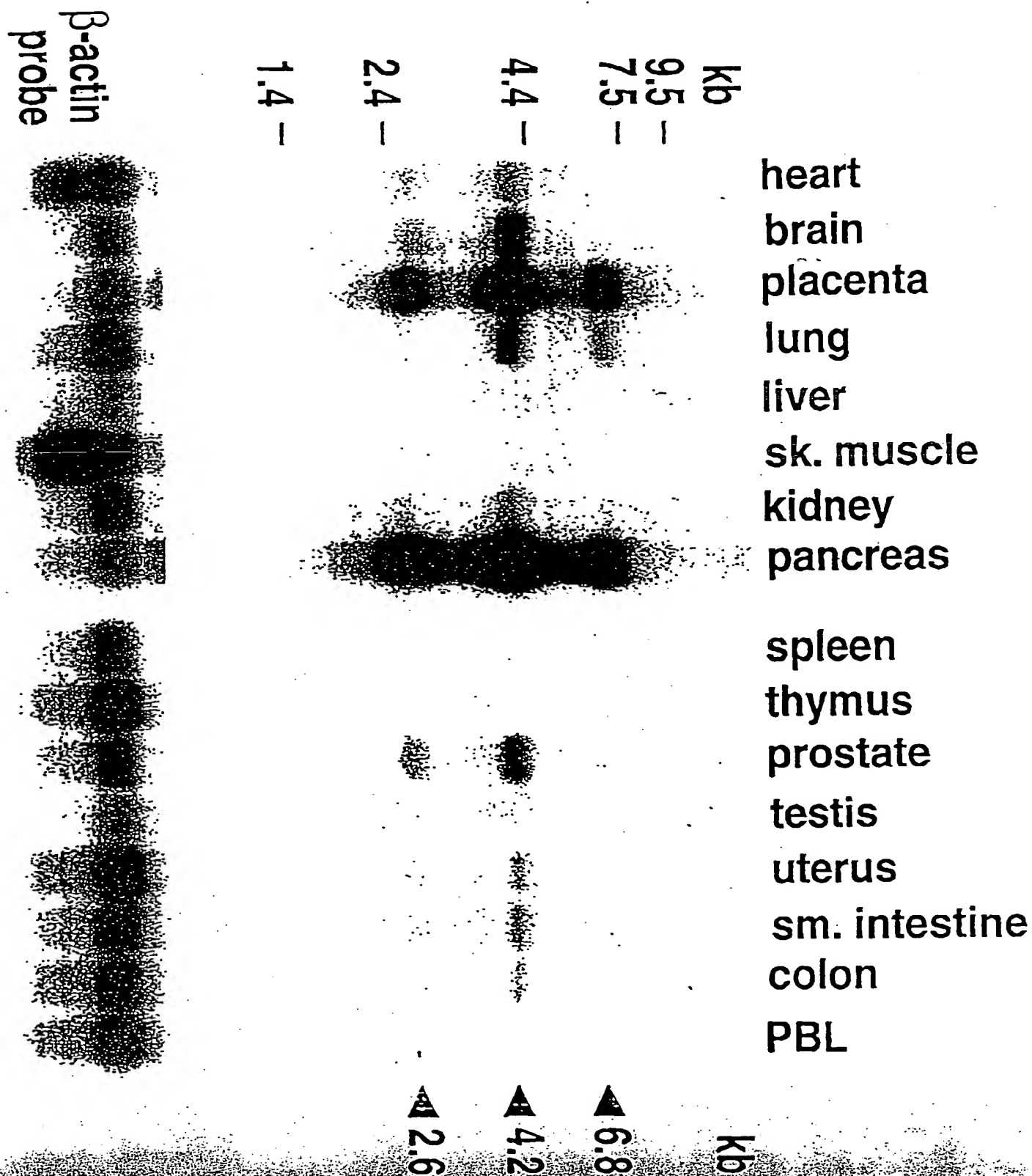
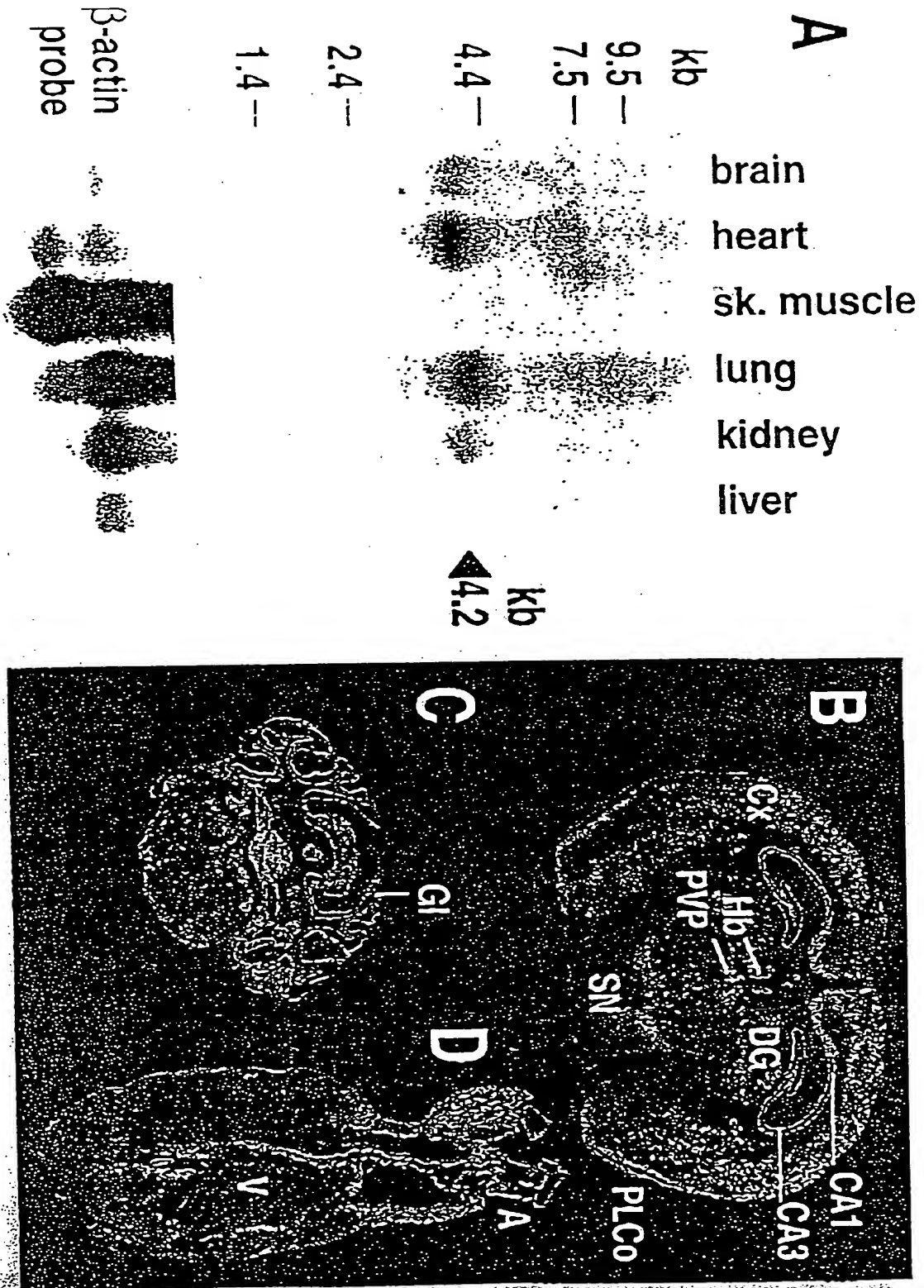


Fig. 11



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Fig. 12

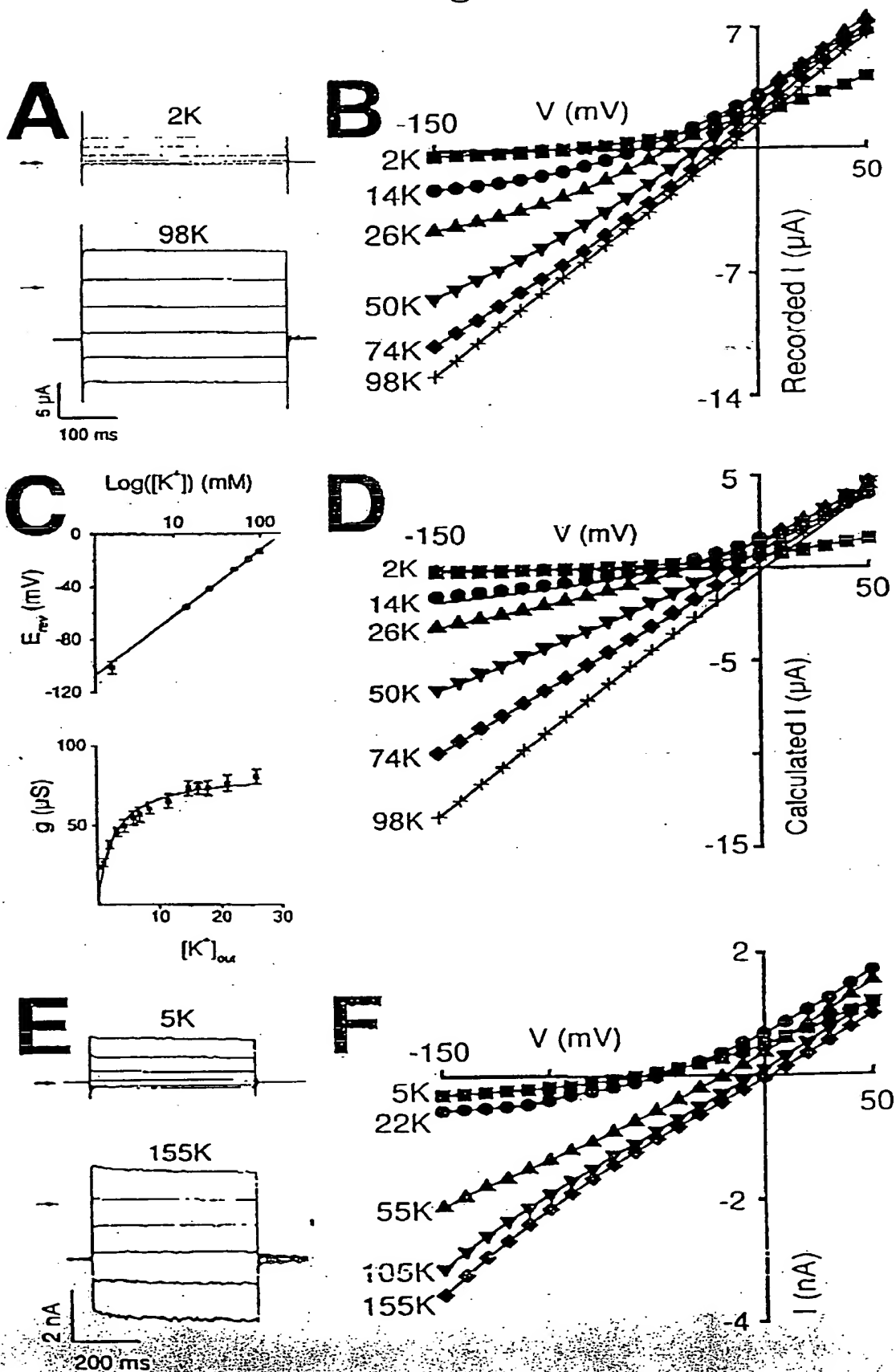


Fig. 13

